

## Two Cases of Adenocarcinoma of Lung in 11-Year-Old Boys and Literature Review

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### 1. Abstract

Lung adenocarcinoma is a non-small cell lung cancer. Adenocarcinoma accounts for about 40% of primary lung tumors. However, there are few reports of primary lung cancer in children. In this report, we describe two children with lung cancer who had never smoked aged 6-12 years, one boy has the first EGFR mutation. In addition, we review similar reports over the past 20 years. Our aim is to provide better recommendations for the treatment and diagnosis of lung adenocarcinoma in children of this age group. Lung cancer is one of the most common causes of adult cancer and the major cause of cancer-related deaths. Nevertheless, the incidence that children have lung cancer is rare. It is suggested that there are one cases in every two million cases, or 0.2% of all children's malignant tumors.1 Adenocarcinoma is the most common lung malignancy in adults and is extremely rare in the pediatric population, accounting for only 8% of lung tumors in children.2 In Asian countries, the incidence of squamous cell carcinoma and small cell carcinoma decreased significantly in both sexes, while the incidence of adenocarcinoma increased significantly in almost all age groups.3.

### 2. Case Reports

#### 2.1. Case 1

An 11 year old boy, six months old, underwent a chest CT scan due to a local physical examination and showed a nodule in the middle lobe of his right lung, no cough and expectoration, no chest tightness, no shortness of breath or fever. No smoking history, family genetic history is not evident, and there is no history of malignancy, no congenital cystic airway mutations. CT showed that the ground glass nodule in the middle lobe of the right lung was

about 6x6mm in size. (Figure 1A). Pathological findings indicate moderately differentiated invasive adenocarcinoma in the peripheral type. (Figure 1B). There were no KRAS or EGFR (epidermal growth factor receptor) mutations. Immunohistochemical staining showed that cytokeratin 7, TTF-1 (Recombinant Transcription Termination Factor, RNA polymerase I), Napsin-A, ki-67(8%) and P63(part) were positive, but negative for ALK-Ventana and CDX2. The right middle lobe wedge resection was performed. Five months after operation, CT showed as shown in the Figure 3A. The patient is now alive and in good condition.

#### 2.2. Case 2

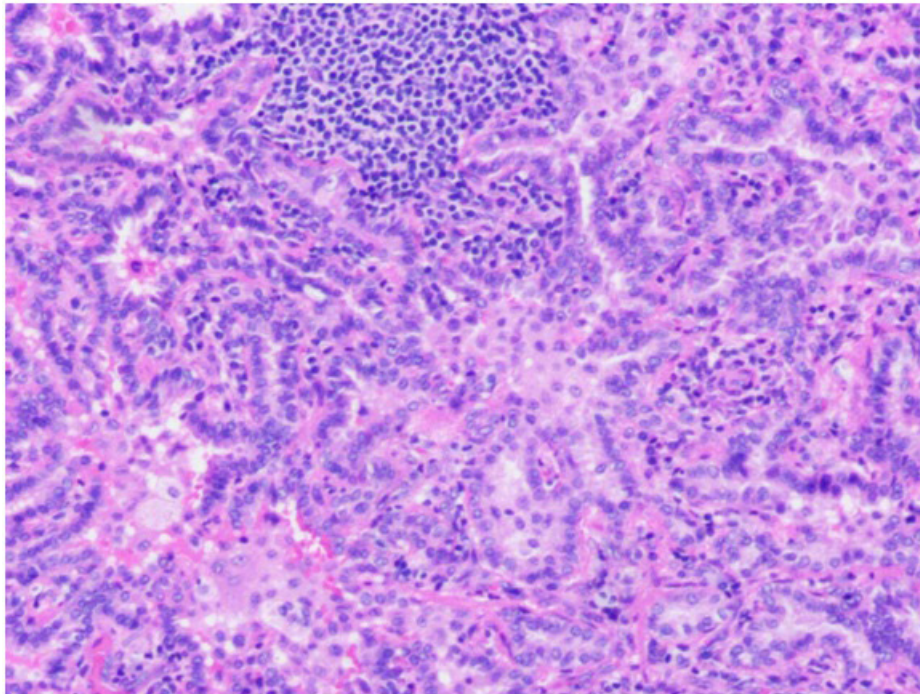
Five years ago, another 11 year old boy also had a chest CT scan because of a physical examination, which showed a nodule in the lower lobe of his right lung. No smoking history, family genetic history is also not evident and there is no history of malignancy, no congenital cystic airway mutations, no cough and expectoration, no chest tightness, no shortness of breath, and no fever. He was not diagnosed with active pulmonary tuberculosis. CT showed part solid nodule in the lower lobe of the right lung was about 6x7mm in size. (Figure 2A). He had WES test that both epidermal growth factor receptor (EGFR) and KRAS were positive. Pathological findings indicate peripheral adenocarcinoma of lung. Immunohistochemical staining showed cytokeratin 7(Figure 2B), TTF-1 (Recombinant Transcription Termination Factor, RNA polymerase I (Figure 2C), Napsin-A(Figure 2D), ki-67(5%) and WT1 (Wilms tumor 1) (Figure 2E) were positive, but negative for ALK-lung. Finally, wedge resection of the right lower lobe was performed. Seventeen months after operation, CT showed as shown in the Figure 3B. The patient is now in good health. Review

of the Literature Literature retrieval using PubMed, terms “adenocarcinoma of lung,” The search was limited to articles describing patients [6-12] years old, and time was from 2000 to 2019. The results and studies are displayed in Table 1. Only one of these patients was localized adenocarcinoma, and the rest were metastatic. They basically have no smoking history. Two children were positive of KRAS+ and MRE11+ respectively. The prognosis of primary lung adenocarcinoma in children is poor [2]. This may be due to the fact that the most have nonspecific symptoms, for example, persistent cough, asthma, hemoptysis, and occasionally metastatic diseases [8]. This can lead to a delay between the presentation of lung cancer in children and the final diagnosis. In this report, the two boys both did not have nonspecific present, however, multiple studies indicated 6% of children with lung cancer are asymptomatic [9]. Incidental findings or permanent imaging abnormalities may also lead to diagnosis [10]. They had the same performance. But there will be a question, what's the size of pulmonary nodule should be followed up or be treated. There are less evident data, and protocols are inferred from adult guidelines. Basically, the diagnosis and treatment of lung adenocarcinoma in kids refer to adult lung cancer guidelines. Fleischner Society indicates for solitary partial solid nodules less than 6 mm in diameter, it is recommended to follow up for 3-6 months, followed by at least 5 years per year, according to the association. For the reported cases,

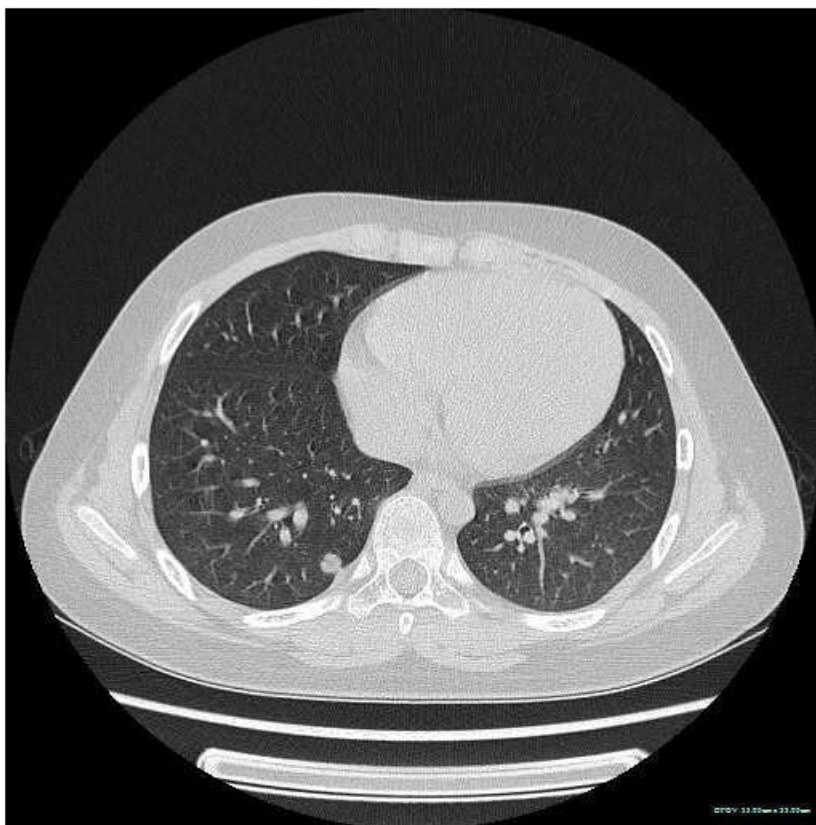
the guideline recommends more follow-up [11,12]. However, two boys both have invasive adenocarcinomas, the guidelines suggest that this type of partially solid nodule of this size is usually MIA or AIS [13]. This may also be due to incomplete lung development or the unique biological behavior of tumors in this age group. The biopsy tissues of children's adenocarcinoma would be tested for various oncogenes, such as ALK, KRAS, Ros1, ERbB2, RET, Met, NTRK1 and EGFR. We are trying to identify specific targeted drugs given to patients with driver gene mutations. What's more important is to determine whether there is a particular driver gene at this age [14]. Related studies have also shown the effectiveness of targeted drugs, but some treatment methods still refer to adult guidelines [15] and its safety and controllability still need to be studied. In fact, the final management is surgery, chemotherapy or radiotherapy. But in the young, the proportion of surgery is increasing [16]. There are also some high-risk factors. Congenital pulmonary airway malformation has been considered as an important factor of lung cancer in children [17]. The lung adenocarcinoma can simulate tuberculosis in imaging study. It is suggested that lung cancer should be included in the differential diagnosis when the symptoms and signs of pulmonary tuberculosis appear in adolescents [18]. However, whether smoking is a high risk factor for children aged 6 to 12 years is too small and most patients deny smoking history. So it's hard to get a scientific proof.



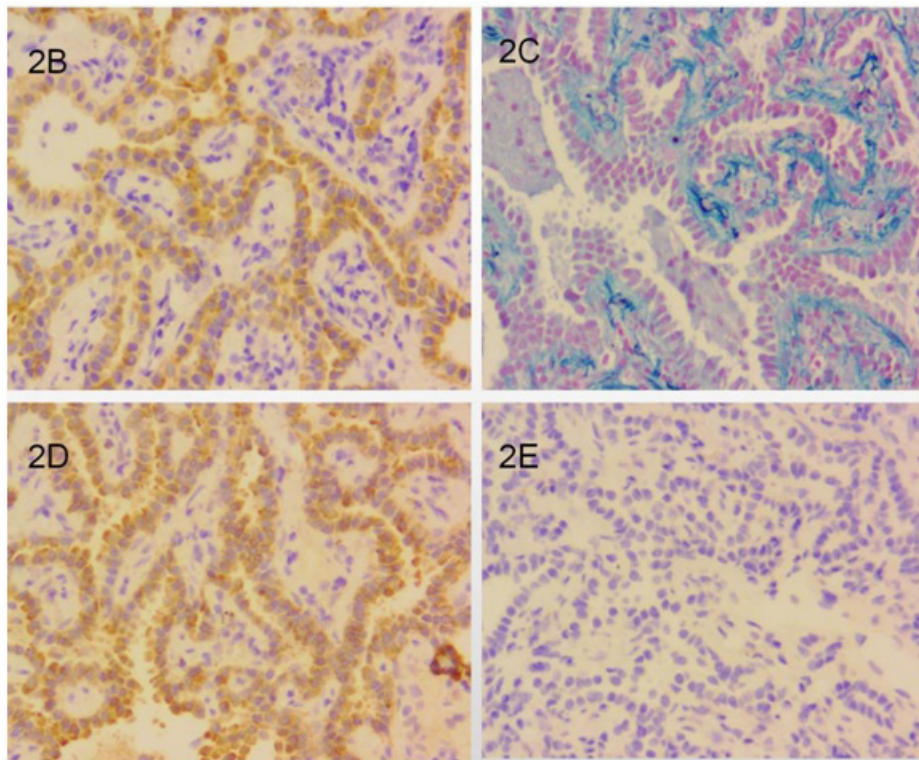
**Figure 1A:** CT showed that the ground glass nodule in the middle lobe of the right lung was about 6x6mm in size.



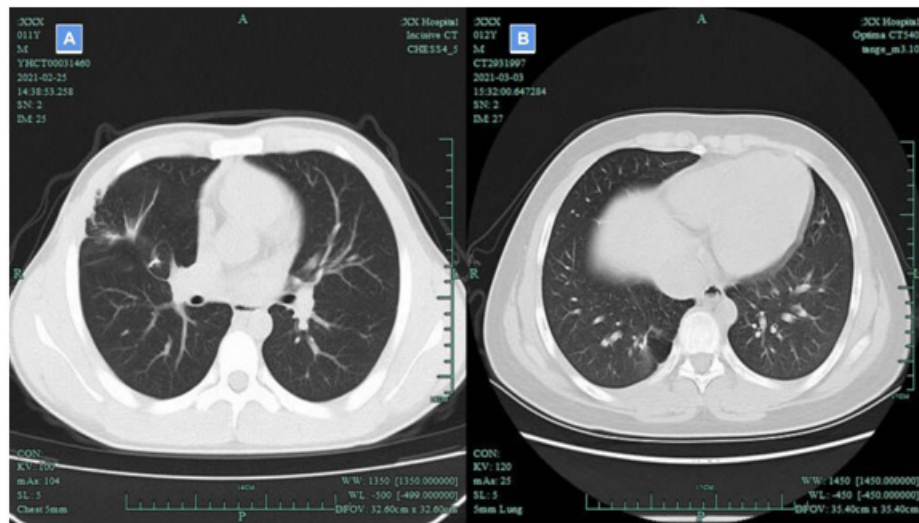
**Figure 1B:** Pathological findings indicate moderately differentiated invasive adenocarcinoma in the peripheral type.



**Figure 2A:** CT showed part solid nodule in the lower lobe of the right lung was about 6x7mm in size.



**Figure 2(B-E):** cytokeratin 7(2B), TTF-1(2C), Napsin-A(2D), ki-67(5%) and WT1(2E).



**Figure 3(A-B):** A: The patient's right middle lobe wedge resection 5 months CT showed no significant abnormalities. B: Wedge resection of right lower lobe for 17 months showed no significant abnormality on CT.

**Table 1:** Characteristics of lung adenocarcinoma Reported in Children

Author	Age/Sex	Additional Cytogenetics	Smoke Exposure	Stage	Treatment	Outcome
Martino <sup>4</sup> 2018	10/F	ALK, EGFR, ROS1 -	No	Extensive	Chemotherapy surgery radiation	Died from disease
Summers <sup>5</sup> 2010	8/F	KRAS +, EGFR-	No	Extensive	Surgery chemotherapy	Alive with disease
Uchisaka <sup>6</sup> 2009	9/M	MRE11 +	No	Extensive	Chemotherapy radiotherapy	Died from disease
DiFurio <sup>7</sup> 2003	10/M	Not available	Unknown	Limited	Surgery	Disease free
Present Study	11/M	Not available	No	Limited	Surgery	Disease free
Present Study	11/M	KRAS, EGFR+	No	Limited	Surgery	Disease free

M, male; F, female, Age (Years), Author (in Reverse Chronological Order). MRE11; meiotic recombination *11* homolog A. KRAS; v-ki-ras2 Kirsten ratsarcoma viral oncogene homolog. EGRF; epidermal growth factor receptor.

### 3. Discussion

In this report, we found the first case of lung adenocarcinoma driven by EGFR gene aged 6-12 years. However, EGFR mutation is found in about 22% of the younger lung adenocarcinoma documentations,<sup>19</sup> the proportion of Asians will be even higher<sup>20</sup>. In children with lung adenocarcinoma, oncogene mutations and molecular screening should be carried out to identify potential targeted mutations and provide a choice for the treatment of specific targeted drugs. However, little is known about primary adenocarcinoma in children, our purpose is to call for more people to study to develop correlative guidelines in 6-12 age group.

### References

- Neville HL, Hogan AR, Zhuge Y. Incidence and outcomes of malignant pediatric lung neoplasms. *The Journal of surgical research*. 2009; 156: 224-30.
- Rojas Y, Shi YX, Zhang W. Primary malignant pulmonary tumors in children: a review of the national cancer data base. *Journal of pediatric surgery*. 2015; 50: 1004-8.
- Kinoshita FL, Ito Y, Nakayama T. Trends in Lung Cancer Incidence Rates by Histological Type in 1975-2008: A Population-Based Study in Osaka, Japan. *J Epidemiol*. 2016; 26: 579-86.
- De Martino L, Errico ME, Ruotolo S. Pediatric lung adenocarcinoma presenting with brain metastasis: a case report. *Journal of medical case reports*. 2018; 12: 243.
- Summers RJ, Shehata BM, Bleacher JC, Stockwell C, Rapkin L. Mucinous adenocarcinoma of the lung in association with congenital pulmonary airway malformation. *Journal of pediatric surgery*. 2010; 45: 2256-9.
- Uchisaka N, Takahashi N, Sato M. Two brothers with ataxia-telangiectasia-like disorder with lung adenocarcinoma. *The Journal of pediatrics*. 2009; 155: 435-8.
- DiFurio MJ, Auerbach A, Kaplan KJ. Well-differentiated fetal adenocarcinoma: rare tumor in the pediatric population. *Pediatric and developmental pathology: the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society*. 2003; 6: 564-7.
- Weldon CB, Shamberger RC. Pediatric pulmonary tumors: primary and metastatic. *Semin Pediatr Surg*. 2008; 17: 17-29.
- Yu DC, Grabowski MJ, Kozakewich HP. Primary lung tumors in children and adolescents: a 90-year experience. *Journal of pediatric surgery*. 2010; 45: 1090-5.
- Giuseppucci C, Reusmann A, Giubergia V. Primary lung tumors in children: 24 years of experience at a referral center. *Pediatr Surg Int*. 2016; 32: 451-7.
- MacMahon H, Naidich DP, Goo JM. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. *Radiology*. 2017; 284: 228-43.
- Silva M, Milanese G, Sestini S. Lung cancer screening by nodule volume in Lung-RADS v1.1: negative baseline CT yields potential for increased screening interval. *Eur Radiol*. 2020.
- Lee JH, Park CM, Lee SM, Kim H, McAdams HP, Goo JM. Persistent pulmonary subsolid nodules with solid portions of 5 mm or smaller: Their natural course and predictors of interval growth. *Eur Radiol*. 2016; 26: 1529-37.
- Luo W, Tian P, Wang Y. Characteristics of genomic alterations of lung adenocarcinoma in young never-smokers. *Int J Cancer*. 2018; 143: 1696-705.
- Besse B, Adjei A, Baas P. 2nd ESMO Consensus Conference on Lung Cancer: non-small-cell lung cancer first-line/second and further lines of treatment in advanced disease. *Ann Oncol*. 2014; 25: 1475-84.
- Youlden DR, Foresto SA, Aitken JF. Primary malignant lung tumors in children: A report from the Australian Childhood Cancer Registry, 1983-2015. *Pediatr Pulmonol*. 2020; 55: 719-22.
- Santosham R, Santosham R, Tirunagari V, Jacob SS. Adenocarcinoma in situ in type I congenital pulmonary airway malformation. *Asian Cardiovasc Thorac Ann*. 2019; 27: 606-8.
- Park JA, Park HJ, Lee JS. Adenocarcinoma of lung in never smoked children. *Lung cancer (Amsterdam, Netherlands)*. 2008; 61: 266-9.
- Schrock AB, Welsh A, Chung JH. Hybrid Capture-Based Genomic Profiling of Circulating Tumor DNA from Patients with Advanced Non-Small Cell Lung Cancer. *Journal of thoracic oncology: official publication of the International Association for the Study of Lung Cancer*. 2019; 14: 255-64.
- Akamatsu H, Katakami N, Okamoto I. Osimertinib in Japanese patients with EGFR T790M mutation-positive advanced non-small-cell lung cancer: AURA3 trial. *Cancer science*. 2018; 109: 1930-8.